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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/013,077	01/26/1998	JEFFREY L. NAUSS		2904

7590 11/18/2002

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EXAMINER
CELSA, BENNETT M

ART UNIT	PAPER NUMBER
1639	34

DATE MAILED: 11/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

file copy

Application No.	Applicant(s)
09/013,077	Naus et al.
Examiner	**Art Unit**
Bennett Celsa	1639

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15, 18, 21-23, 25, 26, 48, and 49* is/are pending in the application.

4a) Of the above, claim(s) *18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15, 21-23, 25, 26, 48, and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *Jan 26, 1998* is/are a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some* c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Continued Prosecution Application

1. **The request filed on June 4, 2002 (paper no. 31) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/013,077 is acceptable and a CPA has been established. An action on the CPA follows.**

DETAILED ACTION

NOTE: the location of the present application is **ART UNIT 1639.**

Status of the Claims

Claims 15, 18, 21-23, 25, 26, 48 and 49 are pending.

Claim 18 is withdrawn from consideration.

Claims 15, 21-23, 25, 26, 48 and 49 are under consideration only to the extent that they read on the elected invention (e.g. compositions of peptides comprising seq. Id. 3).

Election/Restriction

2. Applicant's election without traverse of Group I (claims 15, 21-23, 25, 26, 48 and 49 drawn to compositions comprising a 16 amino acid peptide of seq. Id 3) in Paper No.33 is acknowledged.

3. Claim 18 and the part of claims 15, 21-23, 25, 26, 48 and 49 which are directed to fragments of seq. Id 3 or other sequence id's other seq. Id 3 (e.g. Groups II-XVI) are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claim Objections

4. Claims 21, 22 and 25 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. .

A. In claim 21 (and dependent claim 22), the term "said composition can be used as a vaccine component against pathogenic microorganisms and neoplasms" fails to further limit claim 15 which is drawn to a composition claim e.g. intended use fails to further limit.

B. Claim 25 which is **dependent on claim 49** fails to further limit the subject matter of a **previous** claim (emphasis provided)

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 15, 21-23, 25, 26, 48 and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (NEW MATTER REJECTION). .

A. To the extent that Applicant's amendment (e.g. paper no. 13: dated 6/28/00) of claim 15 can be interpreted to encompass "minimized peptides" beyond those peptides having (e.g. comprising) seq. Id. 3; the increased scope constitutes new matter. Amending the claim to

remove terminology such as "is minimized" and "minimized peptide" (e.g. to recite "... a peptide in which the peptide binds to a class ... etc) will overcome this rejection.

B. To the extent the limitation "peptide comprises **thirteen** amino acids" in claim 23 resulting from Applicant's amendment (e.g. paper no. 22: dated 5/2/01) extends beyond an immunogenic composition comprising a peptide having the **16** amino acid peptide of seq. Id 3; the increased breadth encompassing peptides having 13mer, 14mer and 15mer fragments of seq. Id. 3 constitutes new matter.

With regard to items A. and B. above, it is noted that the specification fails to provide direct support or examples of peptides which are representative of the additional scope; nor has applicant indicated where such specification support exists. Applicant must cancel the new matter in response to this rejection.

7. Claims 15, 21-23, 25, 26, 48 and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunostimulatory composition comprising a peptide having seq. 3 which binds to a Class II MHC receptor DR1 which inhibits the binding of HA residues 306-318 to the receptor, the specification does not reasonably provide enablement for immunogenic compositions for use as a vaccine (e.g. against pathogenic microorganism and neoplasms) . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any experimentation is "undue". These factors include, but are not limited to:

1. The breadth of the claims.

2. The nature of the invention

3. The state of the prior art;

4. The level of one of ordinary skill

5. The level of predictability in the art;

6. The amount of direction provided by the inventor;

7. The presence or absence of working examples;

8. The quantity of experimentation necessary needed to make or use the invention based on the disclosure;

See :*In re Wands* USPQ 2d 1400 (CAFC 1988):

(1-2) The breadth of the claims and the nature of the invention:

Although addressing compositions, intended use of these compositions addresses immunogenicity, which includes immunostimulation but also use as a vaccine against pathogenic microorganism and neoplasms. Accordingly, the claims encompass the prevention of innumerable pathogenic microorganisms including viruses and bacteria as well as any type of cancer. Intended use as a vaccine is broad with regard to potential diseases (e.g. cancers, AIDS, hepatitis etc) and further would encompass any means of administration (e.g. oral, injection etc.) to any organism.

Accordingly, the claim scope is unduly broad with respect to encompassed disease states, modes of administration and host.

(3 and 5) *The state of the prior art and the level of predictability in the art:*

The efficacy of a drug treatment in vivo faces unfavorable obstacles not present in vitro models. As such, in vivo utility necessarily involves unpredictability with respect to physiological activity of an asserted process in humans. See discussion in Ex parte Kranz, 19 USPQ2d 1216,1218-1219 (6/90). For example, drug delivery to the targeted area must survive the acidic environment of the stomach if administered orally. Regardless of the route of administration, the drug if indeed immunogenic as many drugs are, must survive an antibody response which may serve to accelerate the progression of infection or disease. Additionally, the delivery of the drug across necessary cell surfaces in amounts needed to be efficacious, but not lethal to the organism, necessitates sensitive testing in order to adequately determine the proper human dosage. For the difficulties in targeting and delivery of proteins or polypeptides via oral administration and the formulation of efficacious unit dosage forms is recognized in the art (see Yang et al., U.S. Pat. No. 5,424,289 at col. 1). Further, determining the proper dosage for a wide range of active ingredients, avoiding enzymatic degradation upon delivery and successful tissue targeting are just some of the difficulties faced when designing an oral pharmaceutical dosage form.

Applicant's claim scope encompasses obtaining and/or enhancing prevention (e.g. vaccine) of variable disease states of variable etiology. However, the burden of enabling the prevention of a disease (ie. the need for additional testing) would be greater than that of enabling a treatment

due to the need to screen those animals (e.g. humans) susceptible to such diseases and the difficulty of proof that the administration of the drug was the agent that acted to prevent the condition. The specification does not provide guidance as to how one skilled in the art would go about screening those patients susceptible to different disease states. Nor is guidance provided in the specification as to a specific protocol to be utilized in order to prove the efficacy of the presently claimed composition as a vaccine for preventing diseases states generally, or any disease state in particular.

(4) *The level of one of ordinary skill in the art:*

The level of skill would be high, most likely at the Ph.D. level.

(6-7) *The amount of direction provided by the inventor and the existence of working examples.*

There are no examples directed to the presently claimed invention; nor is there any guidance as to dosage regimens, preferred disease states or "vaccination effects" are to be enhanced; nor to how one measures such effects or determine the type or degree of effect which is within the scope of the presently claimed invention.

(8) *The quantity of experimentation needed to make or use the invention based on the content of the disclosure:*

In light of the unpredictability surrounding the claimed subject matter; the undue breadth of the claimed invention's intended use; and the lack of adequate guidance, one wishing to

practice the presently claimed invitation would be unable to do so without engaging in undue experimentation.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 15, 21-23, 25, 26, 48 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Interpretation of claim 15 (& claims dependent thereon) is confusing as to whether "a peptide" present in the composition is a peptide having seq. Id 3 or a "minimized peptide" of seq. Id 3.

B. In claim 21 (and claims dependent thereon) , the term "said composition can be used as a vaccine component against pathogenic microorganisms and neoplasms" is confusing since the limitation implies method steps (e.g. can be used ...) , while the claimed invention is drawn strictly to a composition.

C. In claims 23 and 48, "said peptide" lacks clear antecedent basis. Does the peptide refer to "the minimized peptide" or a peptide having seq. 3 ?

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 15, 21-23 and 48 are rejected under 35 U.S.C. 102(a) as being anticipated by Nauss et al. Journal of Immunology Vol. 150/No. 8 part II, No. 221 (April 15, 1993) in view of specification pages 12-13 to demonstrate inherency.

The Nauss et al. article teaches a synthetic antigenic T-cell epitope of the pilus protein of enterotoxigenic E. Coli (ETEC) representing residues 63-78 of the ETEC CS3 pilus protein (CS3 63-78) which inhibits the binding of radio-labeled synthetic peptide or residues 307-319 of the influenza hemaglutinin protein (HA 307-319) to purified DR1 Class II MHC in a direct binding assay. The T-cell epitope for CS3 pilus protein subunit 63-78 corresponds to Ser-Lys-Asn-Gly-Thr-Val-Thr-Trp-Ala-His-Glu-Thr-Asn-Asn-Ser-Ala (Seq. Id No: 3) of the CS3 protein, as presently claimed thus rendering the Nauss et al. compositions anticipatory regarding the immunogenic compositions presently claimed. See present specification. Intended use (e.g. as a vaccine against various microbes/neoplasms in claims 21-22) in compound/composition claims lack patentable weight. Additionally, to the extent that the reference teaching of the reference peptide being "antigenic" fails to suggest immunogenicity; such characteristics would be deemed to be inherent to the reference composition which contain an antigenic peptide and compositions thereof within the scope of the presently claimed invention.

13. Claims 15, 21-23, 25, 26, 48 and 49 are rejected under 35 U.S.C. 102(e) as being anticipated by Reid et al. U.S. Pat. No. 5,417,986 (5/95: filed 4/92 or earlier) in view of specification pages 12-13 to demonstrate inherency

Reid et al. teach oral/parenteral/intestinal vaccine compositions and their use against diseases caused by enteropathogenic organisms (e.g. E. Coli) using antigens encapsulated within biodegradable-biocompatible microspheres (DL-lactide-co-glycolactide) . See e.g. abstract; col. 3-4; See Examples and Patent claims. The Reid et al. patent further teaches that the CS3 protein is

known; and the use of a CFA/II microsphere vaccine and other immunogenic compositions suggests the presence and use of CS3 protein in such compositions. See e.g. Examples; col 37-38 (especially lines 31-54). The reference teaching of CS3 protein and/or vaccine compositions comprising the CS3 protein anticipate the presently claimed compositions since the CS3 protein necessarily comprises presently claimed Seq. Id 3 since the T-cell epitope for CS3 pilus protein subunit 63-78 corresponds to Ser-Lys-Asn-Gly-Thr-Val-Thr-Trp-Ala-His-Glu-Thr-Asn-Asn-Ser-Ala (Seq. Id No: 3) of the CS3 protein. See present specification. It is noted that intended use (e.g. as a vaccine against various microbes/neoplasms in claims 21-22) in compound/composition claims lack patentable weight

14. Claims 15, 21-23, 25, 26, 48 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nauss et al. Journal of Immunology Vol. 150/No. 8 part II, No. 221 (April 15, 1993) and the specification pages 12-13 to demonstrate inherency in view of Reid et al. U.S. Pat. No. 5,417,986 (5/95: filed 4/92 or earlier) .

The Nauss et al. article teaches a synthetic antigenic T-cell epitope of the pilus protein of enterotoxigenic E. Coli (ETEC) representing residues 63-78 of the ETEC CS3 pilus protein (CS3 63-78) which inhibits the binding of radio-labeled synthetic peptide or residues 307-319 of the influenza hemaglutinin protein (HA 307-319) to purified DR1 Class II MHC in a direct binding assay. The T-cell epitope for CS3 pilus protein subunit 63-78 corresponds to Ser-Lys-Asn-Gly-Thr-Val-Thr-Trp-Ala-His-Glu-Thr-Asn-Asn-Ser-Ala (Seq. Id No: 3) of the CS3 protein, as presently claimed thus rendering the Nauss et al. compositions anticipatory regarding the

immunogenic compositions presently claimed. See present specification. Intended use (e.g. as a vaccine against various microbes/neoplasms in claims 21-22) in compound/composition claims lack patentable weight. Additionally, to the extent that the reference teaching of the reference peptide being "antigenic" fails to suggest immunogenicity; such characteristics would be deemed to be inherent to the reference composition which contain an antigenic peptide within the scope of the presently claimed invention.

The Nauss et al. reference differs from the presently claimed invention in failing to teach incorporating its "antigenic" pilus peptide into a pharmaceutical composition comprising a carrier [e.g. biodegradable-biocompatible microspheres (DL-lactide-co-glycolactide)].

Reid et al. teach oral/parenteral/intestinal vaccine compositions and their use against diseases caused by enteropathogenic organisms (e.g. E. Coli) using antigens encapsulated within biodegradable-biocompatible microspheres (DL-lactide-co-glycolactide) . See e.g. abstract; col. 3-4; See Examples and Patent claims. The use of the microsphere carrier prevents the degrading or complexing with secretory IgA in the intestinal lumen of uncomplexed protein antigens. E.g. See Reid et al. Col. 1, especially lines 35-60.

Accordingly, the Reid et al. patent provides motivation (e.g. prevent degradation and unintended immune complexing) to one of ordinary skill in the art to make pharmaceutical compositions comprising the Nauss et al. "antigenic" pilus peptide in microsphere carriers in order to formulate pharmaceutical compositions capable of use as vaccine compositions against pathogenic microorganisms (e.g. including E. Coli.).

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to incorporate the Nauss "antigenic" pilus peptide into a pharmaceutical composition comprising a carrier [e.g. biodegradable-biocompatible microspheres (DL-lactide-co-glycolactide)] as taught by Reid et al. in order to formulate pharmaceutical compositions intended for use as vaccines against pathogenic microorganisms such as E.Col. .

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 15, 21-23, 25, 26, 48 and 49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,309,669 (10/01).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent claims teach pharmaceutical compositions comprising encapsulated (e.g. biodegradable poly lactide/glycolide) "biologically active agents" including immunogenic (e.g. vaccine) peptides (e.g. antibacterial/antiviral). See e.g. patent claims 1-9. The claims encompass preferred "biologically active agents" which include the CS3 peptide 63-78 corresponding to present sequence id 3 . See col. 32 (especially item "112"); col. 33 (especially item "117"); col. 34 (especially item 133) the selection of which would have been prima facie obvious to one of ordinary skill in the art.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang (art unit 1639), can be reached at (703)306-3217.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1639)

November 18, 2002

BENNETT CELSA
PRIMARY EXAMINER